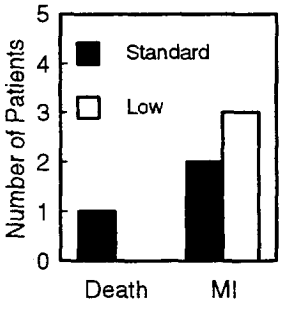
ministered as non-weight adjusted bolus doses to a therapeutic activated clotting time (ACT); bleeding increased with maximal in-lab ACT and relative heparin dose. To evaluate the safety and efficacy of weight-adjusted heparin dosing during c7E3 administration (0.25 mg/kg bolus, 10 mcg/min infusion x 12 hrs), 103 pts undergoing coronary intervention were randomized to 1 of 2 regimens of heparin in a blinded fashion: 100 U/kg bolus + additional doses to achieve ACT > 300 sec (*Standard Dose,* n = 51), or 70 U/kg bolus without ACT adjustment (*Low Dose,* n = 52). ACT values immediately prior to intervention (median and interquartile range) and bleeding complications (unrelated to CABG) during the first 36 hrs (compared to 708 EPIC pts receiving same c7E3 dose), femoral hematoma >5 cm in size, and in-hospital death or MI were:

	EPIC Non Wt-Adjusted Heparin	Standard Wt-Adjusted Heparin	Low Wt-Adjusted Heparin
ACT (sec)	398	330	257
(25th, 75th)	(356, 468)	(308, 374)	(229, 288)
Major bleeds	7.8%	1.9%	2.0%
Minor bleeds	17.9%	7.7%	7.8%
Hematoma	N/A	15.4%	3.9%
Transfusions	15.5%	7.7%	2.0%



Thus, reduced weight-adjusted heparin dosing with c7E3 antiplatelet therapy during coronary intervention in this pilot study did not increase ischemic events, and at the same time appeared to decrease bleeding complications. Weight-adjusted heparin strategies will be further tested in a large-scale, randomized trial (EPILOG).

2:45

711-4 Low Plasma Homocysteine Levels Predict Reduced Atheroma Burden in Patients Undergoing Coronary Interventions: Evidence from Intravascular Ultrasound

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Objectives: Elevated plasma homocysteine (HCY) is an important risk factor for premature coronary atherosclerosis. Intravascular ultrasound commonly demonstrates extensive plaque burden at "normal" reference sites in interventional patients, averaging 38% area reduction. We performed this study to determine if HCY levels predict which patients exhibit diffuse disease involving reference segments.

Methods: We measured plasma homocysteine (μmol/L) in 62 patients undergoing coronary interventions. Intravascular ultrasound was performed with a 30 MHz, 3.5 F probe, examining both target lesions and reference segments. A blinded core laboratory quantified four measures of atheroma burden — maximum and minimum plaque thickness (P_{min} and P_{max}) respectively, plaque cross-sectional area (P_{area}), and percentage cross-sectional area reduction (CSA_{red}).

Results: Measures of atheroma extent and distribution at target lesions were similar in both groups. However, at reference segments:

Reference Segments	P_{min} (mm)	P_{max} (mm)	P_{area} (mm^2)	CSA_{red} (%)
HCY <8 μmol/L	0.18	0.76	4.38	32.3%
HCY >8 μmol/L	0.27	1.04	6.98	40.3%
p value	<0.0005	<0.0001	<0.0001	<0.0012

Strong statistical significance for a protective effect of a low homocysteine level persisted when controlling for age, gender, diabetes, hypertension, cholesterol and smoking in the two cohorts.

Conclusions: In interventional patients, low plasma homocysteine levels independently predict the presence of focal atherosclerosis with sparing of reference segments. These findings have potentially important implications for the clinical approach to intervention.

3:00

711-5 Mechanism of Benefit of Platelet IIb/IIIa Receptor Inhibition in High Risk Angioplasty in the EPIC Trial: A Hierarchical Endpoint Analysis

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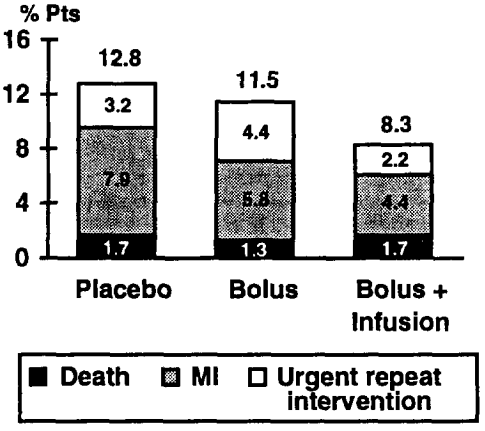
The EPIC trial demonstrated the potent platelet IIb/IIIa inhibitor, c7E3 reduced the incidence of acute complications in high risk angioplasty. The primary endpoint was a composite of death, myocardial infarction (MI), repeat urgent PTCA or CABG, and emergency stent or balloon pump insertion. Event rates were recorded by the *first* occurrence of an endpoint, yet 30% of pts experienced more than one endpoint. To further characterize the mechanism of effect of potent platelet antagonism during angioplasty, we determined c7E3's efficacy according to the *most serious* endpoint reached. Endpoints were ranked hierarchically according to degree of seriousness in the order of death, MI, and urgent intervention. The three treatment groups were placebo, bolus (B) or bolus plus infusion (B + I) of c7E3.

Results: There were no differences in death rates among the 3 treatment groups, (although 2 pts who died in the B + I group never received the drug). Reduction in MI in pts who survived (4.4% B + I vs 7.9% placebo), accounted for 78% of the 4.5% absolute decrease in the composite primary endpoint by B + I (8.3% vs 12.8% placebo p = 0.003). In pts that survived and had no MI, a reduction in urgent repeat intervention (2.2% vs 3.2% for placebo) accounted for only 22% of the overall reduction of the primary endpoint by B + I. Although urgent repeat intervention was less with B + I, the greatest benefit was in pts who also had MI (1.4% vs 4.5% in placebo p < 0.001).



Conclusions: Hierarchical endpoint analysis demonstrates that the mechanism of benefit of c7E3 bolus plus infusion treatment in high risk angioplasty was principally the reduction of MI, rather than a decrease in need for urgent repeat intervention.

3:15

711-6 Declining Resource Utilization in Interventional Cardiology

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While in recent years there has been concern with the cost of interventional cardiology, technical improvements that may have impact to lower resource utilization. Thus, the results of and indices of resource utilization of interventional procedures in 17,263 patients from 1980 through 1993 were reviewed. Previous studies have shown emergency surgery (CABG) and length of stay (LOS) to be the strongest correlates of cost (r = 0.89). Results (mean or %, MV = multivessel, EF = ejection fraction, New Dev = new devices, Ang Suc = angiographic success, Q MI = Q wave myocardial infarction, B/D = number of balloons or devices, LOS in days):